

# Breast Masses and Nipple Discharge

Gretchen Dickson, Crystal L. Jones, and George D. Harris

Breast symptoms are a common problem initiating a woman's visit to a physician's office. The most common symptoms include breast pain (mastalgia), nipple discharge, or a breast mass. Each of these complaints deserves evaluation by a physician. A thorough clinical examination should be performed as part of a complete breast assessment along with specific imaging studies.

Breast pain (mastalgia) is the most frequent breast complaint but only about half of women with breast pain seek medical evaluation. It occurs with multiple conditions but does not have a known etiology. Mastalgia occurs more often during menses and more frequently in premenopausal than in postmenopausal women. Neither hormonal fluctuations nor fluid retention has been shown to cause mastalgia. Hormonal fluctuations related to menstruation or pregnancy are often responsible for breast tenderness. They may also occur during puberty (in females and males), during breastfeeding, or as a woman approaches menopause. The occurrence of breast pain or tenderness in a teenage boy is referred to as gynecomastia and is a normal part of development. Other causes of breast pain include fibrocystic breast disease, mastitis, premenstrual syndrome, alcoholism with liver damage, and local injury or trauma to the breast.

## NIPPLE DISCHARGE

Nipple discharge is the third most common breast complaint. The incidence of symptomatic nipple discharge in patients referred to a breast clinic is between 4.8% and 7.4%. It is not unusual for a woman to express either spontaneously or with external pressure, a physiologic discharge from her breast in the form of a few drops of sticky, gray, green, or black viscous fluid (nonpuerperal galactorrhea). However, any abnormal nipple discharge is a symptom of pathology within the breast and requires further evaluation.

### Symptoms

- Unilateral or bilateral nipple discharge ++++
- May or may not have associated breast mass +++
- Spontaneous or provoked
- Mastalgia

## Signs

- Visible or expressed nipple discharge: The secretion can be bloody, serous, serosanguineous, or watery. ++++
- May or may not have associated breast mass +++
- Spontaneous or provoked
- Breast tenderness may be present if there is an abscess or infection.

## Workup

- A comprehensive, detailed medical history and a physical examination are imperative in the evaluation of a nipple discharge.
- The patient's age, the type and duration of the discharge, pregnancy history, the presence of a mass, history of breast cancer, trauma or other breast conditions, unilateral or bilateral discharge, family history of nipple discharge, and whether the discharge is spontaneous or provoked are important.
- Medication history is also important because various hormones (estrogen, oral contraceptives, thyrotropin-releasing hormone [TRH]), psychotropic medications (risperidone, SSRIs, tricyclic antidepressants), antihypertensives (methyldopa, verapamil), antiemetics (metoclopramide), and H<sub>2</sub>-receptor blockers (cimetidine) can cause increased prolactin levels and galactorrhea.
- A mammogram is indicated in all women with unilateral spontaneous nipple discharge.
- An ultrasound may be the initial modality to evaluate breast abnormality in women younger than age 35.
- Cytology and occasionally biopsy of a nipple discharge and any breast mass, respectively, may be indicated.
- One should perform cytologic examination on all guaiac-positive nipple discharges to evaluate the fluid for breast carcinoma. This procedure is done by placing a glass slide at the ductal opening, expressing the discharge onto the slide, and immediately spraying the slide with a fixative. Up to four slides should be prepared.
  - If the slides test negative for occult blood, the patient should have a prolactin level and TSH performed.
  - If the test is positive for occult blood, then surgical consultation is needed.

## Comments and Treatment Considerations

In nonpregnant or nonlactating women, the more likely diagnosis of nipple discharge includes intraductal papilloma, ductal ectasia, pituitary adenoma, breast abscess or infection, and breast carcinoma.

A mammogram is indicated in all women with unilateral spontaneous nipple discharge. An ultrasound may be the initial modality to evaluate the breast abnormality in women younger than age 35.

A pathologic nipple discharge is usually spontaneous, unilateral, and from a single duct opening on the nipple. The secretion can be bloody, serous, serosanguineous, or watery.

The most common cause of pathologic nipple discharge is a benign intraductal papilloma followed by ductal ectasia. Carcinoma is the least likely cause and occurs in about 10% to 15% of cases.

## BREAST MASS

A breast mass is the most common presenting symptom or complaint in most breast clinics. In these situations a clinical breast examination reveals a palpable dominant breast mass in about half of the possible breast mass cases. However, breast masses are often detected by the patient and are associated with localized swelling, thickening, tenderness, or pain. Breast masses are a common occurrence throughout the life span of a woman.

Even though most breast masses are benign, their diagnostic evaluation should proceed as expeditiously as possible to allow optimal clinical benefit and to alleviate patient fears because for her, this can be one of the most traumatic experiences of her life. A thorough clinical examination should be performed as part of a complete breast assessment along with specific imaging studies. Ultrasonography and mammography are two basic imaging techniques for routine diagnostic imaging of breast diseases. Screening mammography is typically conducted among asymptomatic women and a diagnostic mammogram is usually the first imaging study performed for women older than the age of 35 with a palpable or suspected breast mass.

If a mass is present, ultrasound is also ordered to determine whether the mass is a simple cyst, a complex mass, or a solid mass. It is not clear how much the presence of symptoms increases the risk of breast cancer at screening exams, but studies have shown that the specificity of screening and diagnostic exams may be lower for women with breast symptoms compared with women without symptoms.

Because a breast mass is the most common symptom associated with breast cancer, all masses deserve clinical evaluation. The presence of a breast mass on palpation requires a mammogram, fine-needle aspiration (FNA), and surgical evaluation for excisional biopsy. This approach is necessary because the majority (55% to 68%) of breast cancer cases continue to present with palpable masses, despite the widespread use of screening mammography. The breast mass may be cystic or solid. An ultrasound can be used to distinguish between a solid and cystic lesion.

If the mass is cystic it needs to be confirmed by FNA. If the aspirated fluid is clear and the mass disappears following the aspiration, then the mass is classified as a simple cyst. This site needs to be reevaluated in 4 to 6 weeks for recurrence. Recurrence of the cyst suggests further evaluation with a biopsy or excision of the mass. If the aspirated fluid is grossly positive or positive for occult blood or it does not disappear with FNA, the mass needs cytologic evaluation. The presence of a solid mass requires mammography and a surgical biopsy. The presence of a nonpalpable breast lesion on mammography or ultrasound deserves stereotactic localization and biopsy.

Any persistent palpable breast mass must be diagnosed by FNA and cytology or with histology obtained by tissue core-needle biopsy or open surgical biopsy. Approximately 9% to 11% of breast masses result in the diagnosis of breast cancer.

Breast cancer prevalence among women presenting with a breast mass increases with age (1% for women age 40 or younger, 9% for women between ages 41 and 55, and 37% for women 55 or older). Because diagnosis and treatment options evolve quickly, early referral to a breast surgeon may be indicated. Although the prevalence of breast cancer diagnoses among women with symptoms is low, failure to diagnose breast cancer is one of the most common causes of malpractice claims and results in some of the highest liability awards and payments in medical malpractice.



## FIBROCYSTIC BREAST DISEASE

Fibrocystic breast disease is perhaps one of the most common benign conditions of the breast. Studies suggest that more than 60% of women are affected by this condition at some point in their lives with the most common ages affected being 30 to 50. Because of the associated hormonal influences, it is a much more rare condition after menopause and incidence is lower in women taking oral contraceptive pills.

### Symptoms

- Irregular, dense pebble-like consistency of breast tissue ++++
- Intermittent breast fullness or discomfort
- Dull, heavy pain that occurs in association with menstrual cycles
- Nipple discomfort or itching

### Signs

- Mobile, rubbery mass ++++
- Outer upper quadrant predominance
- Round mass with smooth borders

### Workup

- Breast self-examination
- Clinical breast examination +++
  - Can detect up to 44% of abnormalities alone with up to 29% of those having been missed on mammogram alone
- Ultrasound ++++
  - Under appropriate criteria, sensitivity is 89% with specificity for lesions at 78%
- Mammogram
  - May be difficult to interpret in young women who are generally affected
  - Increased density of breast tissue in disease may further hinder interpretation.
- Biopsy
  - May be needed to rule out other disorders if lesions are large, painful, or persistent
  - Fibrocystic change is often present in histologic studies, although women may be asymptomatic.

- Ultrasound
- Breast self-examination
- Clinical breast examination

### Comments and Treatment Considerations

A placebo effect is common and may account for as much as 20% of improvement.

A well-fitting brassiere may offer support and symptomatic relief and should be worn 24 hours a day for adequate relief.

Dietary modification should include limiting dietary fat intake to 25% of total calories. This will affect the intermediate marker of disease, but still has an unknown effect on symptoms. Eliminate caffeine. There is insufficient evidence to use vitamin E, vitamin B<sub>6</sub>, or evening primrose dietary supplement for relief; however, much anecdotal evidence exists about effect. Typically 400 IU of vitamin E is used, but much variation exists in dosing and preparation of all of these compounds.

Oral contraceptives may limit hormonal effects thought to mediate disease process. Danazol was previously used for severe pain; however, it is being phased out because it has many androgenic side effects. Tamoxifen is noted to reduce fibrocystic breast disease, but only as a side effect when used for reduction of cancer risk.



## FIBROADENOMA

Fibroadenoma is the most common benign breast mass and contains both connective tissue and epithelial elements. Prevalence ranges from 2% to 23% of women and accounts for about half of all breast biopsies occurring most frequently in young women within 20 years of puberty. It has a biphasic incidence with peaks at 25 and 48 years of age. In African American women this is earlier with peaks at 16 and 25 years of age. Younger women tend to have rapid growth of the mass. Multiple lesions may present in 10% to 15% of women. Older women characteristically have a single, slower-growing lesion that frequently calcifies, and may involute after menopause. The etiology is unknown. The diagnosis of fibroadenoma is based on clinical, radiologic, and pathologic examination or a “triple test.” It is not considered cancerous or premalignant and risk factors include a patient who is a postpubescent female or a postmenopausal female exposed to estrogen.

### Symptoms

- Painless, smooth, breast mass ++

### Signs

- Small, well-circumscribed, round or ovoid, rubbery, freely mobile, nontender mass ++
- Usually 1 to 5 cm
- Usually in the upper quadrant

### Workup

- Breast self-examination
- History: Include questions related to nature and pattern of symptoms, relationship to menstrual cycle, timing of onset and course, nipple discharge, hormone use, and any prior treatments
- Clinical breast and axillary examination
- Ultrasound for localization and characterization
  - Most appropriate for women younger than the age of 35 due to breast density
- Mammogram in women older than 35 years for localization and characterization
  - Not appropriate for younger women due to dense breast tissue
- FNA or excisional biopsy +++
  - Diagnostic and definitive treatment

### Comments and Treatment Considerations

Providers must consider fibrocystic condition of the breast and carcinoma in women 30 years of age or older. Triple test: Clinical breast exam, ultrasound, FNA, or core-needle biopsy is used to evaluate fibroadenomas.

No treatment is necessary and the lesion may be observed if benign triple test unless one of the three components is discordant or the lesion enlarges. Conservative management with serial ultrasounds every 6 months is acceptable for stable lesions. Benign fibroadenomas can change size. A change in 20% in any one of the three dimensions over a 6-month interval was not associated with malignancy. Fibroadenomas may increase significantly in size during pregnancy. If the change in size is more significant, the lesion may be associated with malignancy or phylloides tumor. Fibroadenomas may also regress or become smaller. This is more likely in very young women, new-onset lesions, small masses, and those that occur during pregnancy.

If diagnosis is uncertain, excision or vacuum-assisted core needle removal with cytologic examination is recommended. Complex fibroadenomas include epithelial calcification, apocrine metaplasia, sclerosing adenosis, and size larger than 3 mm.

Epithelial hyperplasia with atypia occurs in 0.3% and does not correlate with an additional increased long-term risk of breast carcinoma.

Fibroadenomas may increase the long-term risk of developing breast cancer. There is a 2.17 to 3.1 relative risk in those with a family history of breast cancer and complex fibroadenomas.

Cryoablation and ultrasound-guided vacuum-assisted biopsy are being studied as an alternative to excision. MRI is being studied as a noninvasive and reliable alternative to tissue diagnosis.



## BREAST ABSCESS AND INFECTION

The diagnosis of a breast abscess is characterized by breast pain, redness, tenderness, flulike symptoms, and a fluctuant mass. Breast abscesses are most commonly associated with lactation and occur

within the first month postpartum or at weaning, but may be fistulous tracts from squamous epithelial neoplasm or duct occlusion. Prevalence of breast abscess in breastfeeding women is 0.1%. A breast abscess develops in 5% to 11% of women with mastitis.

Risk factors are maternal age more than 30 years, primiparity, gestational age 41 weeks' or more, mastitis, diabetes, RA, steroids, silicone or paraffin implants, lumpectomy with radiation, heavy cigarette smoking, nipple retraction, history of a bite, or penetrating trauma.

### Symptoms

- Mastalgia +++
- Erythema
- Myalgia
- Malaise
- Fever ++
- Chills ++

### Signs

- Breast tenderness ++++
- Localized swelling or pitting edema
- Localized warmth
- Fluctuant mass
- Usually unilateral +++
- Purulent exudates
- Proximal (axillary) lymphadenopathy

### Workup

- CBC: Helps quantify infection and monitor response to therapy
- Ultrasound: Helps differentiate between mastitis and abscess in addition to localizing the lesion for definitive treatment
- Aspiration: Helps in obtaining culture sample and is also for definitive treatment
- Culture and sensitivity: Help identify the pathogen and sensitivity or resistance to antibiotic therapy
- ESR may be used in monitoring the inflammatory response.

### Comments and Treatment Considerations

#### *Cold Compresses*

Continue expression of milk, if lactating, by pumping on the affected side. Initiate empiric antibiotic therapy with appropriate drugs early. Common etiologic agents include *Staphylococcus aureus*, *Streptococcus*, and *Escherichia coli*. Nonlactational abscesses are associated with anaerobic bacteria. Drugs of choice include first-generation cephalosporin, erythromycin, Augmentin, and clindamycin.

Drainage of the localized abscess can usually be performed by needle aspiration, with or without ultrasound guidance. If needle aspiration is not effective, incision and drainage are needed with the removal of loculations and opening of all fistulous tracts. If the incision does not interfere with latch-on, breastfeeding may

continue on both breasts. If the incision interferes with nursing on the affected breast, a pump should be used to remove milk regularly for 3 to 4 days until the wound is sufficiently healed to allow nursing. Nursing should continue on the unaffected breast. Antiinfective properties of the milk that drains from the abscess may bathe the wound and accelerate healing.

Biopsy should be performed on all nonlactating abscesses to rule out inflammatory carcinoma. NSAIDs should be used for pain relief and to decrease the local inflammatory response.

Treat mastitis early with cold compresses and milk expression if lactating. Follow patient until resolution to exclude carcinoma. Complete healing should be within 8 to 10 days. Relapse occurs in up to 38% of women within an 8-year period and is more associated with those who are not lactating.

Consider mammography and biopsy after infection has cleared.



## GYNECOMASTIA

Gynecomastia results in the most common cause of male breast evaluation throughout the male life cycle with increased prevalence in teenage (10% to 48%) and older adult men (57% of men greater than age 50). Although breast cancer is less common in men, it should be considered if a focal abnormality is present.

### Symptoms

- Enlargement of one or both breasts ++++
- Typically a global enlargement as a mass or lump requires evaluation for other etiologies.
- Breast pain, nipple discharge, or change in nipple size more concerning

### Signs

- Enlargement of breast ++++
  - Can be quite significant
  - Classified into lesions that are less than 5 cm and greater than 5 cm because this correlates with expected resolution and response to treatment

### Workup

- Physiologic gynecomastia does not require workup, however, must ensure that enlargement is physiologic
- Thorough history is critical
- Examine for symptoms related to decreased testosterone production or other diseases.
- Kallmann's syndrome
  - Embryonic absences of GnRH-secreting neurons leading to lack of hypothalamic GnRH
- Klinefelter's syndrome
- Genotype of XXY



- Increased risk of breast cancer from 10% to 20% ++
  - Testicular tumors
  - 5- $\alpha$  reductase deficiency
  - Androgen insensitivity
- Age of onset of gynecomastia
  - Physiologic in newborns, adolescents, and older adult males
- History of mumps or testicular trauma
  - Rule out testicular torsion and viral orchitis
- Use of alcohol or medications
  - Heroin
  - Marijuana
  - Digitalis
  - Phytoestrogens
  - Gonadotropins
  - Clomiphene
  - Phenytoin
  - Ketoconazole
  - Metronidazole
  - Methyldopa
  - Busulfan
  - Tricyclic antidepressants (TCAs)
  - Calcium channel blockers
  - Angiotensin-converting enzyme (ACE) inhibitors
  - Cisplatin
  - Spironolactone
  - Cimetidine
  - Flutamide
  - Finasteride
  - Etomidate
  - Atorvastatin
- Family history of similar changes + + + +
- Infertility or sexual dysfunction
- Thorough physical examination
  - For stigmata of liver, thyroid, or renal disease
  - Look for other signs of feminization such as abnormal body hair or voice tone.
  - Testicular examination
    - Rule out masses or asymmetry
    - Obtain ultrasound if concern exists for neoplasm
- Breast examination
  - Examine size of breasts and consistency of tissue.
    - Gynecomastia is enlargement of glandular tissue and can be treated.
    - Pseudogynecomastia is enlargement of adipose tissue typically noted in those that are obese.
      - This does not warrant treatment other than ongoing encouragement for weight loss.
  - Nipple discharge
  - Axillary lymphadenopathy
  - Obtain a mammogram if a concern exists for male breast cancer.

- Workup then does not significantly differ from that typically followed for females with mass for concerning cancer
- BMP to rule out chronic liver or renal disease
- TSH to rule out hyperthyroidism
- If other features of feminization exist, consider:
  - Total testosterone
    - If elevated check testicular ultrasound
  - Luteinizing hormone (LH)
  - Estradiol
  - Dehydroepiandrosterone sulfate levels
- If no features of feminization exist, instead consider:
  - Total testosterone
    - If elevated check testicular ultrasound
  - LH
  - FSH
  - Prolactin
  - $\beta$ -hCG and estradiol levels
    - If elevated, check chest x-ray and CT of chest, abdomen and pelvis to find primary secreting tumor.

### Comments and Treatment Considerations

Physiologic gynecomastia does not require treatment; 90% of adolescent gynecomastia resolves within weeks to 3 years. If breasts are larger than 4 cm, full regression is less likely.

Treat underlying diseases if gynecomastia is not physiologic. Remove offending medications. Consider replacing testosterone through parenteral or transdermal systems if androgen is low.

Idiopathic or residual gynecomastia can be pharmacologically treated with clomiphene (50 to 100 mg/day for up to 6 months with 50% of patients having reduction in breast size and 20% of patients having full resolution), tamoxifen (10 to 20 mg twice daily with 80% reporting resolution within 3 months), danazol (inhibits LH and FSH to decrease estrogen synthesis, 200 mg twice daily, with complete resolution noted in 23% of cases), or testolactone (150 mg three times daily for 6 months; can cause significant side effects with less than 40% of patients having decrease in breast size).

Reduction mammoplasty can be considered if medical therapy has failed. This option is also considered for cosmetic reasons. Liposuction may be sufficient if pseudogynecomastia is suspected.



### INTRADUCTAL PAPILLOMA

#### Symptoms

- Nipple discharge
  - Often bloody +++
  - Unilateral +++
- Breast mass
  - Typically small, hard nodule ++++
  - Found behind nipple most commonly

- Breast pain +++
- Breast enlargement
  - Unilateral difference in breasts that is of new onset

### Signs

- Bloody or serous nipple discharge +++
  - May be expressed on examination
  - Can be spontaneous
- Breast lump
  - May or may not be palpable by examiner
  - Found behind nipple most commonly

### Workup

- Mammogram
  - Typically not useful because women may be younger with denser breasts
  - Papillomas often not appreciated on mammogram
- Ultrasound
  - Most useful modality
  - Diagnostic features
    - Dense, coarse calcifications
    - Highly vascular
      - Propensity to bleed spontaneously
      - Vascular pedicle may be found
- Ductogram
  - May be useful because contrast can outline papilloma
- Breast biopsy with pathology ++++
  - Cytokeratin stains of biopsy can be useful for differentiating this from other breast lesions.
  - Cell clumping and nuclear change may help differentiate benign and malignant disease.

### Comments and Treatment Considerations

Surgical excision is required to aid in symptom control and remove papilloma. Typically local area excision of affected duct can be undertaken. Wide surgical excision is not typically needed.



## IN SITU LOBULAR OR DUCTAL CARCINOMA

Ductal carcinoma in situ (DCIS) is a noninvasive premalignant breast disease that is diagnosed by pathologic examination of tissue specimens. DCIS is considered a precursor to invasive ductal carcinoma (IDC), the most common histologic type of invasive breast cancer. DCIS carries a 2- to 8.6-fold increased risk of invasive breast cancer. DCIS is diagnosed in up to 20% of breast cancer patients.

Lobular carcinoma in situ (LCIS) is noninvasive and now also considered a premalignant breast disease based on pathologic exam of tissue specimens. LCIS is considered a precursor to invasive lobular carcinoma (ILC) and carries a 3- to 4.2-fold increased risk of invasive breast cancer.

There is difficulty in classification alone due to the fact that histologic criteria differentiating ductal carcinoma in situ from atypical ductal hyperplasia and similarly lobular carcinoma in situ from atypical lobular hyperplasia are not strongly established. DCIS is further differentiated by comedo or non-comedo classifications.

Non-comedo is the most common histologic type of DCIS and thought to be the precursor to comedo or poorly differentiated or high-grade DCIS. Despite the problem with correct classification of each lesion, the incidences of both have been increasing. The yearly incidence of DCIS is 4.5 to 5.4/1000 and has increased 7.2-fold, with the highest rates of increase in women 50 years of age and older and non-comedo classifications increasing while comedo DCIS is decreasing. IDC rates have remained constant. The yearly incidence of LCIS is 5.2 to 7.3/1000 and has increased 2.6-fold, primarily among older women. In addition, ILC rates have also increased (65%) and similarly vary with age. This may be a factor of screening practices, skills, technology, and the increased use of mammography.

Risk factors are similar in both instances and are similar to the risk factors for invasive carcinomas: family history of breast cancer, previous breast biopsy, nulliparity, fewer full-term pregnancies, older at first full-term pregnancy, older at menopause, and ethnicity (African American and Hispanic).

### Symptoms

- Ductal—With or without palpable breast mass or nipple changes  
+++
  - May complain of itching or burning of the nipple
  - Previously presented with palpable breast mass and/or nipple discharge
- Lobular—With or without palpable breast mass

### Signs

- Ductal—With or without palpable breast mass
  - May have superficial erosion or ulceration of the nipple
- Lobular—With or without palpable breast mass

### Workup

- Breast self-examination
- Family history
- Clinical breast examination
- Routine screening mammography (picks up majority of the diagnosed cases, most of which are nonpalpable breast masses) +++
- Ultrasound for localization and characterization of any abnormalities found on mammography
- Large-core needle biopsy, especially in lesions with associated microcalcifications
- Excisional biopsy ++++

### Comments and Treatment Considerations

Those with a family history of breast cancer have a two- to three-fold associated risk, especially if multiple first-degree relatives have

been diagnosed with breast or ovarian cancer and at younger ages. These families have a high correlation to the *BRCA1* and *BRCA2* alleles but there have not been any studies investigating the prevalence of these gene mutations with in situ breast carcinomas.

LCIS lacks any clinical signs and is almost always an incidental finding in breast biopsies that have been done for other reasons. Though not to have any specific findings, it is associated with calcifications on mammography (21% to 67%).

It is hypothesized that postmenopausal hormones are a risk factor for LCIS based on studies showing an associated increased risk for ILC and molecular similarities between ILC and LCIS.

E-cadherin, a cell adhesion molecule, is not expressed in almost all ILCs and is used to distinguish lobular from ductal carcinomas. Loss of expression seems to occur early in the development in ILCs. LCIS has been shown to have complete loss of e-cadherin expression.

There remains no good way to differentiate those who will go on to develop invasive breast cancer from those who will not. DCIS patients are currently recommended for total mastectomy or lumpectomy with radiation. Axillary dissection is not routinely indicated.

Local recurrence rates are higher in those treated with lumpectomy alone and lumpectomy with radiation. This is still controversial given that the majority of DCIS patients will not develop invasive breast cancer.

LCIS is considered a nonsurgical disease and appropriate treatment remains controversial. Options include observation, lumpectomy, chemoprevention with a selective estrogen receptor modulator, or prophylactic mastectomy.

Studies have shown that LCIS patients have the same likelihood to develop invasive tumors in the ipsilateral breast as they do in the contralateral breast, making bilateral mastectomy the best treatment option, which would be unnecessary in up to 80% of patients.



## INFILTRATING (INVASIVE) DUCTAL CARCINOMA (IDC)

Invasive breast cancer accounts for approximately 75% to 85% of breast malignancies with the majority (85%) being IDC. It starts in the duct of the breast and spreads to the fatty tissue of the breast. It may metastasize through the lymphatic system or bloodstream. IDC is an invasive adenocarcinoma that demonstrates differentiation characteristics of breast ductal cells. Histologic diagnostic criteria includes: (1) irregular infiltration of stroma, (2) variable ductal formation by infiltrating cells, (3) a wide range of cytologic atypia and mitotic rates, and (4) the absence of myoepithelial cells in the invasive areas.

Infiltrating carcinoma should be separated from ductal carcinoma in situ by the minimal stromal invasion (microinvasion).

## Symptoms

- A mass that has changed in size +++
- Painless palpable mass
- Breast pain or deformity
- Nipple discharge +++
- Breast erythema
- Breast skin ulceration
- Bone pain, dyspnea, or meningitic syndrome may suggest distant metastases requiring a more extensive workup.

## Signs

- A malignant mass that is firm and hard, usually painless (8% to 90%), irregular, and fixed to the skin or chest wall ++++
- Skin dimpling (the result of shortening or retraction of the Cooper ligaments induced by the tumor; does not have prognostic value)
- Nipple changes or retraction
- Bloody nipple discharge
- Peau d'orange (reflects the invasion of the subdermal lymphatic plexus and lends to a shortened survival)

## Workup

- These lesions should undergo the triple test—a combination of careful, clinical examination, breast imaging, and needle biopsy (pathologic evaluation).
- Nonscystic breast masses in women younger than 40 years of age are common and most often benign.
- No matter what her age, malignancy must be considered in any woman presenting with a dominant breast mass.
- If imaging studies reveal no suspect findings for a patient with an equivocal result on clinical breast examination, repeat breast examination should be scheduled in 6 to 8 weeks.
- Diagnostic mammography should be obtained before biopsy if clinical concern of malignancy is high.
- Negative imaging studies do not eliminate the need for further evaluation of a suspect mass.
- After breast imaging, a needle biopsy—either a core or FNA—should be performed.
- Ultrasound can be used to determine if the mass is solid or cystic along with the use of FNA biopsy. ++++
- Fine-needle aspiration biopsy (FNAB) of the breast is a well-established method for the diagnosis of breast carcinoma. +++++
- The presence of nonbloody fluid and complete resolution of the cyst can confirm its benign nature. However, if the fluid is bloody or the cyst does not resolve after aspiration or has a complex appearance on the ultrasound image, a biopsy is indicated.
- Mammography can provide signs suggestive of cancer that include architectural distortions, microcalcifications, or masses. These changes require further evaluation using diagnostic mammograms with or without ultrasound. Biopsies are indicated if these changes are confirmed.

## Comments and Treatment Considerations

Invasive ductal carcinomas have the poorest prognosis of all invasive breast cancers. The patient and physician must discuss the benefits and risks of mastectomy compared with those of breast conservation therapy (BCT) in each individual case.

Women whose breasts are preserved have more positive attitudes about their body image and experience fewer changes in their frequency of breast stimulation and feelings of sexual desirability. Patients can be offered BCT followed by local irradiation, modified-radical mastectomy alone, or modified-radical mastectomy with immediate reconstruction.

Women with two or more primary tumors in separate quadrants of the breast or with diffuse, malignant-appearing microcalcifications are not considered candidates for BCT. Persistent positive margins after reasonable surgical attempts absolutely contraindicate BCT with radiation.

A history of therapeutic irradiation to the breast region that, combined with the proposed treatment, would result in an excessively high total radiation dosage to a significant volume is an absolute contraindication. Adjuvant systemic therapy should be considered for most women with invasive breast cancer.

Adjuvant tamoxifen citrate similarly substantially reduces the rate of local recurrence in patients treated with breast conservation surgery and local irradiation, but does not seem to reduce greatly the rate of local recurrence after breast conservation surgery alone.



## INVASIVE LOBULAR CARCINOMA

ILC constitutes the second most frequent type of invasive breast cancer accounting for approximately 5% to 10% of invasive breast carcinomas. Invasive lobular carcinomas are characterized by multifocality in the ipsilateral breast and appear to be bilateral more often than other types of invasive breast cancer. Invasive lobular carcinomas show distinctive cytologic features and patterns of tumor cell infiltration of the stroma. In their classic form there are relatively uniform neoplastic cells that invade the stroma singly, resulting in the formation of linear strands that encircle mammary ducts in a target-like manner.

There are variant forms of ILC (solid, alveolar, and tubulolobular), which differ from the classic form with regard to architectural or cytologic features. In the variant forms, the cells comprising the lesion have features characteristic of the classic form, but differ with regard to the growth pattern of the tumor cells. Classical invasive lobular carcinomas typically show expression of estrogen and progesterone receptors.

## Symptoms

- A mass that has changed in size
- Painless palpable mass +++

- Breast pain or deformity
- Tender, thickened area over the breast

### Signs

- Discrete, firm mass on palpation
- Spiculated mass on mammogram
- Only a vague area of thickening or induration, without definable margins
- Abdominal pain

### Workup

- A breast mass should undergo the triple test—A combination of careful, clinical examination, breast imaging, and needle biopsy (pathologic evaluation).
- If imaging studies reveal no suspect findings for a patient with an equivocal result on clinical breast examination, repeat breast examination should be scheduled in 6 to 8 weeks.
- Ultrasound can be used to determine if the mass is solid or cystic along with the use of FNAB. +++
- Diagnostic mammography should be obtained before biopsy if clinical concern of malignancy is high. ++++
- After breast imaging, a needle biopsy—either a core or FNA—should be performed. +++++

### Comments and Treatment Considerations

Metastases to the lungs, liver, and brain parenchyma appear to be less common in patients with lobular than ductal cancers. Lobular carcinomas have a greater propensity to metastasize to the leptomeninges, peritoneal surfaces, retroperitoneum, GI tract, and reproductive organs than do ductal cancers.

The patient and physician must discuss the benefits and risks of mastectomy compared with those of BCT in each case. Patients can be offered BCT followed by local irradiation, modified-radical mastectomy alone, or modified-radical mastectomy with immediate reconstruction.

Women whose breasts are preserved have more positive attitudes about their body image and experience fewer changes in their frequency of breast stimulation and feelings of sexual desirability.

Women with two or more primary tumors in separate quadrants of the breast or with diffuse, malignant appearing microcalcifications are not considered candidates for BCT. Persistent positive margins after reasonable surgical attempts absolutely contraindicate BCT with radiation.

A history of therapeutic irradiation to the breast region that, combined with the proposed treatment, would result in an excessively high total radiation dosage to a significant volume is an absolute contraindication. Adjuvant systemic therapy should be considered for most women with invasive breast cancer. Adjuvant tamoxifen citrate similarly substantially reduces the rate of local recurrence in patients treated with breast conservation surgery and local irradiation, but does not seem to reduce greatly the rate of local recurrence after breast conservation surgery alone.





## INFLAMMATORY CARCINOMA

Inflammatory carcinoma is an aggressive but fortunately rare disease, accounting for 1% to 5% of breast cancers. It has a sudden onset and a rapidly progressive course. It is a distinct form of breast cancer that warrants special clinical considerations. It must be diagnosed promptly to avert progression and death. Because of its aggressive and rapid course, it carries a higher morbidity and mortality than the invasive cancers. It has distinct clinicopathologic features characterized by an early age at diagnosis, poor nuclear grade, negative hormone receptor status, and an overall poor survival outcome.

Inflammatory carcinoma occurs mainly in premenopausal women and is associated with a 95% risk of distant metastases. It is characterized clinically by redness and erythema involving more than half the breast and pathologically by tumor involving the dermal lymphatics of the breast.

Inflammatory breast carcinoma must be distinguished from a common lactational mastitis or abscess. This is usually accomplished by sampling the skin by tissue biopsy at the time the area is incised and drained.

In contrast to inflammatory breast cancer, mastitis often presents with fever, leukocytosis, and systemic malaise. In addition, antibiotics tend to be of immediate benefit in mastitis and breast abscess, but not with inflammatory breast cancer.

### Symptoms

- Discoloration (red to purple) of the skin affecting at least one third of the breast with rapid onset (weeks to months) ++++
- Thickening and/or fine dimpling (peau d'orange) of the skin with rapid onset (weeks to months) ++++
- Warmth and a palpable ridge present at the margin of induration
- Erythematous, nonblanchable nodules over the chest
- Mastalgia (breast pain) +++
- Ecchymosis
- Bone pain

### Signs

- Nipple inversion or retraction +++
- Diffuse erythema
- Breast edema
- Skin ridging (peau d'orange) ++++
- May not be an underlying palpable mass
- Fine dimpling of the skin
- Warmth over the skin
- Palpable or matted axillary lymph nodes
- No distinct mass (occurs in 50% of cases) +++

### Workup

- Biopsy of the affected skin
- Diagnostic mammogram

- Breast ultrasound
- Assess for metastatic disease for patients who are asymptomatic outside the breast. These studies include a bone scan and CT scan of the chest and abdomen.
- The diagnostic workup must include marking the original tumor bed for future radiotherapy planning and other evaluations.

### Comments and Treatment Considerations

The patient and physician must discuss the benefits and risks of mastectomy compared with those of BCT in each case. Chemotherapy with a modified radical mastectomy plus radiotherapy may be an alternative to a radical mastectomy.

Metastases are the major determinant of survival in patients with inflammatory breast cancer. Urgent and aggressive treatment with neoadjuvant anthracycline-based chemotherapy is the current standard for initial treatment.

The neoadjuvant chemotherapy is followed by multimodality locoregional therapy.

### References

- Arisio R, Cuccorese C, Accinelli G, et al: Role of fine-needle aspiration biopsy in breast lesions: analysis of a series of 4,110 cases, *Diagn Cytopathol* 18:462–467, 1998.
- Arpino G, Allred DC, Mohsin SK, et al: Lobular neoplasia on core-needle biopsy-clinical significance, *Cancer* 101:242, 2004.
- Berens PD: Prenatal, intrapartum, and postpartum support of the lactating mother, *Pediatr Clin North Am* 48:365, 2001.
- Boni R: Tumescient power liposuction in the treatment of the enlarged male breast, *Dermatology* 213:140–143, 2006.
- Bradley, SJ, Weaver, DW, Bouwman, DL: Alternatives in the surgical management of in situ breast cancer. A meta-analysis of outcomes, *Am Surg* 56:428, 1990.
- Braunstein GD, Glassman HA: Gynecomastia, *Curr Ther Endocrinol Metab* 6:401–404, 1997.
- Carter BA, Page DL, Schuyler P, et al: No elevation in long-term breast carcinoma risk for women with fibroadenomas that contain atypical hyperplasia, *Cancer* 92(1):30–66, 2001.
- Choi YD, Gong GY, Kim MJ, et al: Clinical and cytologic features of papillary neoplasms of the breast, *Acta Cytol* 50:35–40, 2006.
- Claus, EB, Stowe, M, Carter D: Breast carcinoma in situ: risk factors and screening patterns, *J Natl Cancer Inst* 93:1811, 2001.
- Dener C, Inan A: Breast abscesses in lactating women, *World J Surg* 27:130, 2003.
- Dupont WD, Page DL, Parl FF, et al: Long-term risk of breast cancer in women with fibroadenoma, *N Engl J Med* 331:10, 1994.
- Fisher B, Bryant J, Dignam J, et al: Tamoxifen, radiation therapy, or both for prevention of ipsilateral breast tumor recurrence after lumpectomy in women with invasive breast cancers of one centimeter or less, *J Clin Oncol* 20:4141, 2002.
- Fitzgibbons PL, Henson DE, Hutter RV: Benign breast changes and the risk for subsequent breast cancer: an update of the 1985 consensus statement. Cancer Committee of the College of American Pathologists, *Arch Pathol Lab Med* 122:1053, 1998.
- Foster, MC, Helvie, MA, Gregory, NE, et al: Lobular carcinoma in situ or atypical lobular hyperplasia at core-needle biopsy: is excisional biopsy necessary, *Radiology* 231:813, 2004.

- Frykberg, ER, Bland, KI: Management of in situ and minimally invasive breast carcinoma, *World J Surg* 18:45, 1994.
- Ganesan S, Karthik G, Joshi M, et al: Ultrasound spectrum in intraductal papillary neoplasms of breast, *Br J Radiol* 79, 843–849, 2006.
- Glass AR: Gynecomastia, *Endocrinol Metab Clin North Am* 23:825–837, 1994.
- Gordon PB, Gagnon FA, Lanzkowsky L: Solid breast masses diagnosed as fibroadenoma at fine-needle aspiration biopsy: acceptable rates of growth at long-term follow-up, *Radiology* 229:233, 2003.
- Greenberg R, Skornick Y, Kaplan O: Management of fibroadenoma, *J Gen Inter Med* 13:640, 1998.
- Hammons KB, Edwards RF, Rice WY: Golf-inhibiting gynecomastia associated with atorvastatin therapy, *Pharmacotherapy* 26:1165–1168, 2006.
- Hance KW, Anderson WF, Devesa SS, et al: Trends in inflammatory breast carcinoma incidence and survival: the surveillance, epidemiology, and end results program at the National Cancer Institute. *J Natl Cancer Inst* 97:966–975, 2005.
- Harris J, Lippman M, Morrow M, Osborne C: *Diseases of the breast*, 3rd ed. Philadelphia, 2004, Lippincott Williams & Wilkins.
- Harris GD, White RD, Carlson B, Sisodia T: *Common breast problems*. Monograph, Edition No. 259, Home study self-assessment program. Leawood, KS, 2000, American Academy of Family Physicians.
- Hussain AN, Policarpio C, Vincent MT: Evaluating nipple discharge, *Obstet Gynecol Surv* 61:278–282, 2006.
- Jacobs TW, Connolly JL, Schnitt SJ: Nonmalignant lesions in breast cancer core needle biopsies: to excise or not to excise, *Am J Surg Pathol* 26:1095, 2002.
- Jones DJ, Holt SD, Surtees P, et al: A comparison of danazol and placebo in the treatment of adult idiopathic gynecomastia: results of a prospective study in 55 patients, *Ann R Coll Surg Engl* 72:296–298, 1990.
- Karstrup S, Solvig J, Nolsøe CP, Nilsson P, et al: Acute puerperal breast abscesses: US-guided drainage, *Radiology* 188:807, 1993.
- King TA, Carter KM, Bolton JS, Fuhrman GM: A simple approach to nipple discharge, *Am Surg* 10:960–965, 2000.
- Kuijper A, Mommers EC, Van der Wall E, et al: Histopathology of fibroadenoma of the breast, *Am J Clin Pathol* 115:736, 2001.
- Kvist LJ, Rydhstroem H: Factors related to breast abscess after delivery: a population-based study, *BJOG* 112:1070, 2005.
- Li CI, Daling JR, Malone KE: Age-specific incidence rates of in situ breast carcinomas by histologic type, 1980 to 2001, *Cancer Epidemiol Biomarkers Prev* 14:1008, 2005.
- Li CI, Malone KE, Saltzman BS, et al: Risk of invasive breast carcinoma among women diagnosed with ductal carcinoma in situ and lobular carcinoma in situ, 1988–2001, *Cancer* 106:2104, 2006.
- Mahoney CP: Adolescent gynecomastia. Differential diagnosis and management, *Pediatr Clin North Am* 37:1389–1404, 1990.
- Moriya T, Kasajima A, Ishida K, et al: New trends of immunohistochemistry for making differential diagnosis of breast lesions, *Med Molec Morphol* 39:8–13, 2006.
- Morrow M: Evaluation of common breast problems, *Am Fam Physician* 61:2371–2378, 2000.
- Morrow M, Wong S, Venta L: The evaluation of breast masses in women younger than forty years of age, *Surgery* 124:634–641, 1998.
- Neuman JF: Evaluation and treatment of gynecomastia, *Am Fam Physician* 55:1835–1844, 1849–1850, 1997.
- O'Hara RJ, Dexter SP, Fox JN: Conservative management of infective mastitis and breast abscesses after ultrasonographic assessment, *Br J Surg* 83:1413, 1996.
- Plourde PV, Kulin HE, Santner SJ: Clomiphene in the treatment of adolescent gynecomastia. Clinical and endocrine studies, *Am J Dis Child* 137:1080–1082, 1983.

- Schwarz RJ, Shrestha R: Needle aspiration of breast abscesses, *Am J Surg* 182:117, 2001.
- Sperber F, Blank A, Metser U, et al: Diagnosis and treatment of breast fibroadenomas by ultrasound-guided vacuum-assisted biopsy, *Arch Surg* 138:796, 2003.
- Thompson DF, Carter JR: Drug-induced gynecomastia, *Pharmacotherapy* 13:37-45, 1993.
- Ullitzsch D, Nyman MKG, Carlson RA: Breast abscess in lactating women: US-guided treatment, *Radiology* 232:904, 2004.
- Varey AHR, Shere MH, Cawthorn SJ: Treatment of loculated lactational breast abscess with a vacuum biopsy system, *Br J Surg* 92:1225, 2005.
- Weinstein D, Strano S, Cohen P, et al: Breast fibroadenoma: mapping of pathophysiologic features with three-time-point, contrast-enhanced MR imaging-pilot study, *Radiology* 210:233, 1999.
- Wilkinson S, Anderson TJ, Rifkind E, et al: Fibroadenoma of the breast: a follow-up of conservative management, *Br J Surg* 76:390, 1989.